Preparation of 2-Methyl-4,4-diphenyl-Δ^2-γ-butyrolactone (7). 2-Methyl-3-carbomethoxy-4,4-diphenyl-3-butenoic acid was prepared by the method described in the literature.[27]

A solution of 21.5 g of the above acid, 330 ml of acetic acid, 215 ml of 49% hydrobromic acid, and 108 ml of water was refluxed for 6 hr. The acidic portion was worked up in the usual way and recrystallization from a methanol–water mixture gave a 21.2% yield of 2-methyl-4,4-diphenyl-3-butenoic acid, mp 104.5–105°. The infrared spectrum showed a broad band 3500∼2500 (broad) and 1720 (s) cm^{-1}; nmr (CCl_4) 7.7–7.0 (10 H, multiplet, aromatic), 6.06 (H, doublet, vinyllic hydrogen), 3.6–3.0 (H, multiplet, tertiary hydrogen), 1.29 ppm (3 H, doublet, 7 cps, methyl).

Bromine (1 ml) was added slowly to a solution of 0.194 g of the above acid in 50 ml of saturated aqueous solution of bicarbonate. The mixture was stirred at room temperature for 1 hr and extracted with ether. The ethereal solution was washed with water and dried over magnesium sulfate. The ether was removed by distillation leaving a solid residue. Recrystallization of the residue from pentane gave a 92.8% yield of 2-methyl-3-bromo-4,4-diphenylbutyrolactone, mp 130–132°. The ir spectrum (CCl_4) showed a characteristic lactone absorption at 1800 cm^{-1} (s). The nmr spectrum (CCl_4) showed that the lactone was a mixture of cis and trans isomers: 5.45 (0.355 H, doublet, 4 cps, benzylic) and 4.63 (0.644 H, doublet, 12 cps, benzylic), 7.9–7.15 (10 H, multiplet, aromatic), 3.15–2.5 (1 H, multiplet, α-hydrogen), 1.34 (3 H, doublet, 7 cps, methyl).

A solution of 0.43 g of the above lactone, 1 g of potassium hydroxide, 30 ml of methanol, and 9 ml of water was refluxed for 3.5 hr. The methanol was distilled off, a small amount of ice water was added, and the reaction mixture was acidified with cold dilute hydrochloric acid and extracted with ether. The ethereal layer was washed with saturated aqueous sodium bicarbonate and water and dried over magnesium sulfate. Removal of the ether gave **7**, which after recrystallization from pentane had mp 68–69°.

Isolation of Methyl 1-Methyl-2,2-diphenylcyclopropanecarboxylate. The neutral portion which was separated from the decomposition of **2** in methanol was chromatographed on an alumina column. The alumina was eluted with low-boiling petroleum ether until no more material was found in the solvent. After evaporating the solvent, the methyl ester was collected by vpc using a 2-ft 20% CES on Chromosorb W column at 125°, in a yield of 27.7%, mp 89–90°. The ir and nmr spectra were identical with those of an authentic sample which was prepared from methyl methacrylate and diphenyldiazomethane. A mixture melting point gave no depression.

Decomposition of 2 in Carbon Tetrachloride. The procedures for decomposition, separation of the neutral fraction, isolation of **5**, and quantitative analysis of the products by vpc were the same as described in the general procedure. 1-Chloro-1-methyl-2,2-diphenylcyclopropane was isolated by the following procedure: the neutral portion of the reaction mixture was chromatographed on an alumina column using low-boiling petroleum ether as an eluent. Upon evaporation of the petroleum ether, the residue solidified to yield 19.3% of 1-chloro-1-methyl-2,2-diphenylcyclopropane, mp 65–65.5°. The infrared and nmr spectra were identical with those of an authentic sample.[2,3] A mixture melting point gave no depression. Decomposition of (+)-**2**, $[\alpha]_{Hg}^{23}$ 5.1 (70.3% optical purity, prepared from (−)-**4**, $[\alpha]_{Hg}^{23}$ 30.0) gave (−)-1-chloro-1-methyl-2,2-diphenylcyclopropane, $[\alpha]_{Hg}^{23}$ 1.05 (*c* 2.85, $CHCl_3$).

Decomposition of 2 in Benzene-d_6. The procedures for the decomposition of the peroxide and the isolation of the cyclopropyl hydrocarbon fraction were the same as described in the general procedure. Mass spectrum of the product showed *m/e* 209 ($C_{16}H_{15}D^+$, base peak), 210 (P + 1, relative intensity 21.4%).

---

[27] A. M. McAbbady and H. H. Muosa, *Can. J. Chem.*, 43, 928 (1965).

A Kinetic and Equilibrium Study of the Hydrogen Bond Dimerization of 2-Pyridone in Hydrogen Bonding Solvents[1]

G. G. Hammes* and P. J. Lillford

Contribution from the Department of Chemistry,
Cornell University, Ithaca, New York 14850. *Received April 20, 1970*

Abstract: Rate and equilibrium constants for the hydrogen bond dimerization of 2-pyridone in chloroform–dimethyl sulfoxide (DMSO) and in CCl_4–DMSO mixtures at various DMSO concentrations have been determined by ultrasonic attenuation, ultraviolet, infrared, and nmr measurements. For the former solvent system, the association rate constants were characteristic of a diffusion-controlled process ($k_f \sim 10^9\ m^{-1}\ sec^{-1}$). The equilibrium dissociation constants increased with increasing DMSO content of the solvent, suggesting that the dissociation rate constant is a measure of solvent competition for hydrogen bonds. The values of standard enthalpy changes for the reactions, calculated from the ultrasonic data, also support this interpretation: $\Delta H°$ changes from −6 to −4 kcal/mol as DMSO is increased from 0.67 to 2.26 *m*. For the latter solvent system, very different behavior is observed. The association rate constant is $<10^9\ m^{-1}\ sec^{-1}$ in all cases, indicating that the formation of dimers is not diffusion controlled. The dissociation rate constant increases to a limiting value of $\sim 3.3 \times 10^8\ sec^{-1}$ as the DMSO content is increased. A mechanism, involving 2-pyridone–DMSO complexes, is postulated and leads to the conclusion that solvation–desolvation of 2-pyridone by DMSO becomes rate limiting. The implication of these findings for biological processes is considered.

The hydrogen bond is a significant factor in the structure and function of biological macromolecules.[2-4] Many equilibrium studies have been made of both biological and model systems. Relatively recently, the dynamics of these interactions have also been studied and information is now available on the rates of formation and breakdown of most types of commonly occurring hydrogen bonds.[4] Virtually all the kinetic data have been obtained by studies of the dimerization of simple chemical compounds such as benzoic acid,[5] ϵ-caprolactam,[6] and analogs of the bases of nucleic

---

* To whom correspondence should be addressed.

[1] This work was supported by a grant from the National Institutes of Health (GM 13292).

[2] W. Kauzmann, *Advan. Protein Chem.*, 14, 1 (1959).

[3] G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," Reinhold, New York, N. Y., 1960.

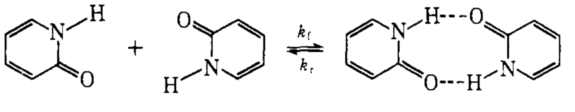
[4] G. G. Hammes, *Advan. Protein Chem.*, 23, 1 (1968).

[5] W. Maier, *Z. Elektrochem.*, 64, 132 (1960); L. Borucki, *Ber. Bunsenges. Phys. Chem.*, 71, 504 (1967).

[6] K. Bergmann, M. Eigen, and L. de Maeyer, *ibid.*, 67, 819 (1963).

acid.[7-9] By necessity, these studies have been performed in inert (CCl_4)[5,6] or relatively weak hydrogen bonding solvents (chloroform, dioxane, 1 wt % water–dioxane).[7-9] A more appropriate environment for models of biological systems is water, but thus far the unfavorable thermodynamics of self-association in water have precluded use of this medium. The rates associated with the helix–coil transition in poly-L-ornithine have been measured in methanol–water mixtures.[10] However, although hydrogen bond formation and breakdown is involved, the data do not directly yield rate constants for the formation and breakdown of a single hydrogen bond.

In principle, the study of simple processes gives the most unambiguous results with respect to the rates of elementary steps associated with hydrogen bonding. This work is concerned with the self-association of 2-pyridone to form a dimeric species stabilized by two hydrogen bonds.



(1)

Although this process could not be studied in highly polar, strongly hydrogen bonding solvents such as water or dimethyl sulfoxide (DMSO), it was found that if the DMSO was diluted with chloroform or carbon tetrachloride the dimerization could be studied. Equilibrium studies were carried out with nmr, ultraviolet, and infrared techniques, and kinetic studies with ultrasonic attenuation measurements. The results indicate that in $CHCl_3$–DMSO mixtures the rate of dimerization is diffusion controlled, while the rate of dissociation increases as the dimethyl sulfoxide concentration increases. On the other hand, the overall rate of dimerization is *not* diffusion controlled in CCl_4–DMSO mixtures A mechanism consistent with all of the data postulates that dissociation of the dimethyl sulfoxide–2-pyridone hydrogen bond becomes rate limiting in this solvent system.

Experimental Section

Materials. Chloroform (Mallinckrodt A.R.) was dried and freed from preservative ethanol immediately before use by passage through a column of aluminum oxide (Woelm, basic activity 1). Carbon tetrachloride (Mallinckrodt A.R.) was stored over molecular sieve (Linde, type 4A) and further purified by passage through a similar alumina column. Dimethyl sulfoxide (Fisher, spectroanalyzed) contained about 0.01% water and was used without further purification. 2-Pyridone (Aldrich reagent grade) was purified by vacuum sublimation. One careful sublimation was usually sufficient to obtain a white powder, mp 110° (lit. 106–107°).

Methods. The apparatus used for making ultrasonic measurements has been described previously.[11] The ultrasound pulse of the required frequency was generated with a Matec 6000 Generator/Receiver (R.F. Plug-In 960). The procedure for measuring the ultrasonic absorption coefficient, α, is the same as described previously,[11] except that changes in received signal intensity were measured with a Matec 1235A Pulse Amplitude Monitor.

Values for the association constants for dimerization of 2-pyridone in carbon tetrachloride and chloroform–dimethyl sulfoxide mixtures were obtained by measurement of the ultraviolet spectrum of dilute solutions of 2-pyridone in the appropriate solvents. A wide concentration range was studied, using cells of 1- and 10-mm path length. Optimum spectral changes were observed at 330 and 335 nm for carbon tetrachloride and chloroform–dimethyl sulfoxide mixtures, respectively. Absorbancy measurements were made using a Cary 14 or Zeiss PMQ II spectrophotometer, thermostated at 25 ± 0.1°. Stoppered cuvettes were used for all measurements and care was taken that the samples were not contaminated with atmospheric moisture. Dimer association constants in CCl_4–DMSO mixtures were too small to be measured by this technique; approximate values were obtained by measurement of the change in chemical shift of the N_1 proton of 2-pyridone with increasing concentration. Chemical shifts were measured with reference to tetramethylsilane (δ 0.0), and calibrated by the singlet methyl absorption of DMSO at δ 2.62. Experiments were performed using a Varian A-60A nmr machine, thermostated at 25 ± 1°.

Hydrogen bond formation between 2-pyridone and DMSO in carbon tetrachloride was measured by infrared spectroscopy. The free S=O group vibration was observed at 1070 cm^{-1}. A Perkin-Elmer SP 21 grating spectrophotometer, fitted with potassium bromide cells of 0.1-mm path length, was used. No thermostating was available with this instrument, and spectra were recorded at 25 ± 3°. The proportions of monomeric and dimeric 2-pyridone in the kinetic samples were monitored by observation of their carbonyl stretching frequencies at 1680 and 1660 cm^{-1}, respectively.

Results and Treatment of Data

The following solutions showed no chemical relaxation in the frequency range 10–165 MHz (*i.e.*, the ultrasonic absorption coefficient, α, divided by the square of the frequency, f, was a constant in each case): pure DMSO, $CHCl_3$, and CCl_4; 2-pyridone in DMSO up to 2 *m*; 2-pyridone (0.5 *m*) in 50 wt % DMSO–$CHCl_3$; mixtures of 0.674, 1.42, and 2.26 *m* DMSO in $CHCl_3$; and freshly prepared mixtures of 0.77, 1.1, 2.2, 3.3, and 5.5 *m* DMSO in CCl_4. Samples of these last solutions showed a decrease in α/f^2 with increasing frequency when contaminated with moisture, and great care was necessary in the preparation and handling of all solutions to exclude water from this solvent mixture.

On the addition of 2-pyridone (0.03–0.5 *m*) to the mixed solvents, data were obtained which, at any given solute concentration, were consistent with the occurrence of a single relaxation process and could be described by eq 2,[12,13] where A and B are constants, ω

$$\alpha/f^2 = \frac{A\tau}{1 + (\omega\tau)^2} + B \tag{2}$$

($2\pi f$) is the angular frequency, and τ is the relaxation time. Alternatively, a single relaxation process can be described in terms of the chemical absorption per wavelength μ_{ch}[12] ($2\alpha_{ch}v/f$) (eq 3), where $\mu_m = Av/2\pi$ and v is

$$\mu_{ch} = 2vf(\alpha/f^2 - B) = \frac{2\mu_m\omega\tau}{1 + (\omega\tau)^2} \tag{3}$$

the ultrasonic velocity.

A plot of log μ_{ch} *vs.* log f passes symmetrically through a maximum when $f = 1/(2\pi\tau)$. The ultrasonic parameters μ_m and τ were obtained by the template technique of Piercy and Subrahmanyam.[14] This analysis requires a known value of B (the infinite frequency value of α/f^2) and for some of the studies of 2-pyridone in DMSO–$CHCl_3$ mixtures the relaxation time was too short for a reliable experimental determination of B. In such

---

[7] G. G. Hammes and H. O. Spivey, *J. Amer. Chem. Soc.*, **88**, 1621 (1966).

[8] G. G. Hammes and A. C. Park, *ibid.*, 90, 4151 (1968).

[9] G. G. Hammes and A. C. Park, *ibid.*, **91**, 956 (1969).

[10] G. G. Hammes and P. B. Roberts, *ibid.*, **91**, 1812 (1969).

[11] J. J. Burke, G. G. Hammes, and T. B. Lewis, *J. Chem. Phys.*, **42**, 3520 (1965).

[12] M. Eigen and L. de Maeyer, *Tech. Org. Chem.*, **8** (2), 895 (1963).

[13] K. F. Herzfeld and T. A. Litovitz, "Absorption and Dispersion of Ultrasonic Waves," Academic Press, New York, N. Y., 1959.

[14] J. E. Piercy and S. V. Subrahmanyam, *J. Chem. Phys.*, 42, 4011 (1965).

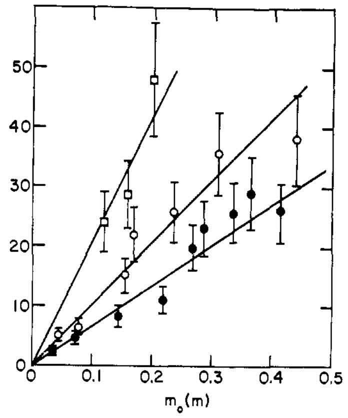


Figure 1. Square of the reciprocal relaxation time (τ^{-2}) *vs.* stoichiometric 2-pyridone molality (m_0) in the presence of: 0.67 *m* DMSO (●), 1.42 *m* DMSO (○), 2.26 *m* DMSO (□). The error bars correspond to a ±10% error in τ. The straight lines were determined by a least-squares analysis of the data.

cases eq 2 was rearranged to give eq 4 and a weighted

$$\frac{1}{\Delta} = [\alpha/f^2 - (B + \Delta B)]^{-1} = \frac{1}{A\tau} + \frac{\tau}{A}\omega^2 \qquad (4)$$

least-squares analysis was carried out using $1/\Delta$ and ω^2 as variables. Since *B* can be experimentally determined in dilute solution, an initial estimate of the parameter *B* was made by extrapolation of a plot of *B vs.* solute concentration for each solvent mixture. Using a computer program developed previously,[7] small changes of *B* (ΔB) were made, and *A* and τ calculated for each *B* value. The best fit was taken to be the value of *B* at which a minimum standard deviation in τ and *A* was obtained.

The ultrasound parameters measured in $CHCl_3$–DMSO and CCl_4–DMSO mixtures are given in Tables I and II, respectively. The experimental error in τ is estimated to be ±10%, except for very short relaxation times where a computer fit was necessary, and for the longest relaxation times where the amplitude of the chemical absorption was small compared with the absorption of the solvent. In these cases the error in τ is probably about ±15%. The error in μ_m for $CHCl_3$–DMSO mixtures (Table I) is ±15% except for very short relaxation times where ±20% is a better estimate. In CCl_4–DMSO mixtures (Table II) the amplitude of the chemical process was found to be extremely sensitive to atmospheric moisture contamination, particularly for the longer relaxation times. For this system the error in μ_m is approximately ±20%.

Table I. Ultrasonic Parameters for 2-Pyridone Dimerization in Chloroform–Dimethyl Sulfoxide Mixtures at 25°

DMSO, *m*	2-Pyridone, *m*	$10^{-8}/\tau$, $\sec^{-1}$	$10^{17}B$, $\sec^2/cm$	$10^{-5}v$, cm/sec	$10^3\mu_m$
0.674	0.037	1.57	220	0.994	1.40
	0.073	2.17	218	0.994	2.48
	0.145	2.83	210	0.996	2.60
	0.218	3.33	200	0.996	3.80
	0.263	4.46	197	1.006	5.20
	0.286	4.81	179	1.020	6.70
	0.333	5.06	178	1.031	6.17
	0.363	5.40	178	1.040	5.60
	0.414	5.10	173	1.060	7.62
1.42	0.044	2.27	142	1.004	1.00
	0.077	2.51	137	1.015	1.90
	0.155	3.90	135	1.037	3.20
	0.233	5.08	136	1.040	6.50
	0.309	5.98	132	1.050	5.90
	0.439	6.18	122	1.087	6.00
	0.167	4.73	137	1.020	4.70
2.26	0.118	4.90	105	1.029	1.20
	0.153	5.35	100	1.069	3.20
	0.200	6.91	98	1.086	4.00

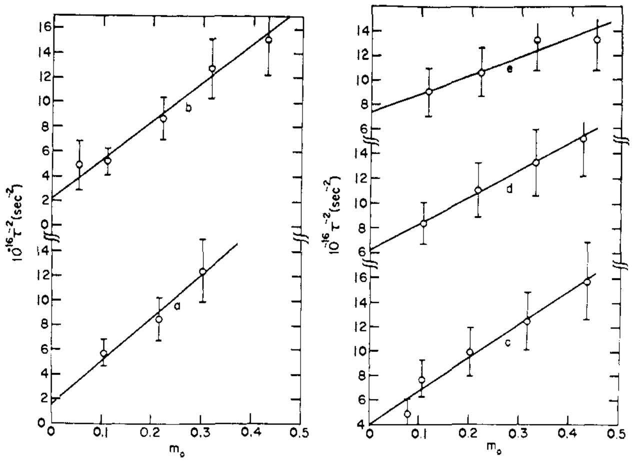


Figure 2. Square of the reciprocal relaxation time (τ^{-2}) *vs.* stoichiometric 2-pyridone molality (m_0) in the presence of: 0.77 *m* DMSO (a), 1.1 *m* DMSO (b), 2.2 *m* DMSO (c), 3.3 *m* DMSO (d), and 5.5 *m* DMSO (e). The straight lines were determined by a least-squares analysis of the data.

Table II. Ultrasonic Parameters for 2-Pyridone Dimerization in Carbon Tetrachloride–Dimethyl Sulfoxide Mixtures at 25°

DMSO, *m*	2-Pyridone, *m*	$10^{-8}/\tau$, $\sec^{-1}$	$10^{17}B$, $\sec^2/cm$	$10^{-5}v$, cm/sec	$10^3\mu_m$
0.77	0.104	2.39	280	0.969	1.6
	0.212	2.89	266	0.973	2.7
	0.301	3.52	255	0.979	3.5
1.1	0.053	2.20	246	0.996	1.1
	0.109	2.26	242	0.998	2.0
	0.218	2.95	225	0.998	4.1
	0.316	3.58	220	1.004	5.5
	0.426	3.90	205	1.007	6.8
2.2	0.055	2.20	174	1.024	1.6
	0.107	2.76	174	1.024	2.2
	0.202	3.14	166	1.029	3.3
	0.314	3.52	160	1.034	4.2
	0.432	3.96	155	1.035	5.0
3.3	0.106	2.89	138	1.069	1.5
	0.215	3.33	130	1.070	2.6
	0.333	3.64	125	1.076	3.6
	0.425	3.90	115	1.075	4.2
5.5	0.114	3.02	104	1.151	1.1
	0.219	3.27	104	1.150	1.04
	0.329	3.64	101	1.165	1.5
	0.450	3.64	100	1.171	1.5

For a simple dimerization process such as that described by eq 1, the reciprocal relaxation time is given by eq 5,[12] where m_M is the equilibrium concentration of

$$1/\tau = k_r + 4k_f(m_M) \qquad (5)$$

the monomer. Equation 5 may be squared and rearranged to give eq 6, where m_0 is the total stoichiometric concentration of 2-pyridone. The data obtained in this work are plotted according to eq 6 in Figures 1 and

$$1/\tau^2 = k_r^2 + 8k_fk_r(m_0) \qquad (6)$$

Table III. Rate Constants and Thermodynamic Parameters for 2-Pyridone Dimerization in Chloroform–Dimethyl Sulfoxide Mixtures at 25°

DMSO, m	0.0[a]	0.67	1.42	2.26
$10^{-9}k_f$, m^{-1} sec^{-1}	3.3	3.2	2.6	2.2
$10^{-7}k_r$, sec^{-1}	2.2	2.6	5.1	12.0
K, m^{-1}	150	124	50	18
$10^3\beta$, deg^{-1}	1.27	1.25	1.22	1.16
ρ, g/cc	1.49	1.45	1.43	1.41
c_p, cal/g deg	0.23	0.23	0.26	0.28
$-\Delta H^\circ$, kcal/mol[b]	5.9	6.1 (±1.2)	5.3 (±1)	4.4 (±0.9)

[a] Reference 9. [b] Average value from different 2-pyridone concentrations; the maximum deviations from the average are given in parentheses.

Table IV. Rate Constants and Thermodynamic Parameters for 2-Pyridone Dimerization in Carbon Tetrachloride–Dimethyl Sulfoxide Mixtures at 25°

DMSO, m	0.0	0.77	1.1	2.2	3.3	5.5
$10^{-8}k_f$, m^{-1} sec^{-1}		3.4	2.6	1.7	1.13	0.69
$10^{-8}k_r$, sec^{-1}		1.22	1.48	2.0	2.5	2.7
K,[a] m^{-1}		2.8	1.7	0.86	0.45	0.25
K,[b] m^{-1}	1650	4	2	0.7	0.25	0.15
$[\Delta V^\circ - (\beta\Delta H^\circ/\rho c_p)]$,[c] cc/mol		9 (±1)	10 (±4)	12 (±4)	12 (±5)	10 (±4)
$10^3\beta$, deg^{-1}		1.25	1.19	1.17	1.14	1.09
ρ, g/cc		1.55	1.54	1.49	1.46	1.41
c_p, cal/g deg		0.223	0.236	0.260	0.280	0.324
ΔH°,[c] kcal/mol		2.5 (±0.3)	3.1 (1±.5)	4.0 (±1.3)	4.3 (±1.5)	4.2 (±2.0)

[a] Calculated from ultrasonic data. [b] Determined by nmr measurements except for the value for pure carbon tetrachloride which was obtained by ultraviolet spectroscopy. [c] Average values from different 2-pyridone concentrations; the maximum deviations from the average are given in parentheses.

2. The concentration scale used in this work is molality, where the solvent is assumed to be either $CHCl_3$ or CCl_4. At high concentrations of DMSO, an alternative procedure is to assume that the solvent is the DMSO–$CHCl_3$ or DMSO–CCl_4 mixture in calculating the molality of 2-pyridone. This latter procedure yields lower concentrations (a maximum of 20%) and gives quantitatively different rate and equilibrium constants. However, these differences are small and do not alter any of the mechanistic considerations discussed later. In the absence of information to the contrary, all activity coefficients are assumed to be concentration independent.

The results obtained in $CHCl_3$–DMSO mixtures, shown in Figure 1, only provide a good determination of $8k_rk_f$ (the slope of the lines) since the intercept on the ordinate is too small to give a reliable estimate of k_r. Hence neither k_r nor k_f can be obtained directly from the ultrasonic data, and an independent determination of the association constant, k_f/k_r, was necessary. This was done by measurements of the ultraviolet absorption of 2-pyridone at various concentrations. The absorption at 335 nm of 2-pyridone does not obey Beer's law, since the extinction coefficients of monomeric and dimeric species are different at this wavelength. The association constant for dimerization can be related to the difference in extinction coefficients ($\Delta\epsilon$) and the deviation from Beer's law (Δa) by eq 7, where m_0 is the

$$K = \frac{\Delta a/\Delta\epsilon}{[(m_0) - 2\Delta a/\Delta\epsilon]^2} \qquad (7)$$

stoichiometric concentration of 2-pyridone. A value of $\Delta\epsilon$ was chosen which gave a minimum standard deviation in the calculated value of K over the concentration range studied. The results are summarized in Table III. The minimum standard deviations were about ±15%; however, the accuracy of the constants is probably somewhat less than this. Using this value of K and the slope of the corresponding line in Figure 1, k_f and k_r were calculated and are given in Table III.

The amplitude of the ultrasonic relaxation process, μ_m, can be written to a good approximation as eq 8,[12]

$$\mu_m = (\rho v^2\pi\Gamma/10^3RT)(\Delta V^\circ - \beta\Delta H^\circ/\rho c_p)^2 \qquad (8)$$

where ρ is the density of the solution, R is the gas constant, ΔV° and ΔH° are the standard volume and enthalpy changes for the reaction, c_p is the specific heat of the solution, and β is the coefficient of thermal expansion for the solvent. For a simple dimerization reaction such as that given by eq 1

$$\Gamma = (1/8K)\{[(1 + 4Km_0)/(1 + 8Km_0)^{1/2}] - 1\} \qquad (9)$$

where K is the association constant.

Strictly speaking, only the quantity $(\Delta V^\circ - \beta\Delta H^\circ/\rho c_p)$ can be determined from μ_m. However, in nonaqueous solvents very often $\Delta V^\circ \ll \beta\Delta H^\circ/\rho c_p$ and, for the dimerization of 2-pyridone in $CHCl_3$–DMSO, ΔV° was assumed to be negligible. The values of ΔH° (averaged from the different concentrations) calculated on this basis are included in Table III. Values of β and ρ were determined experimentally for each solvent mixture; c_p was calculated as the weighted mean of the values for chloroform (0.234 cal/g deg) and DMSO (0.7 cal/g deg). The values of these quantities are included in Table III. Although the sign of ΔH° cannot be determined from ultrasonic data, in these cases it can be safely assumed to be negative.

In CCl_4–DMSO mixtures, the data, plotted according to eq 6, can be used to obtain values of k_f and k_r directly; the rate constants obtained are given in Table IV. In the case of the data at high DMSO concentrations, the experimental error is such that it cannot be said with certainty that the relaxation time is actually concentration dependent; *i.e.*, the kinetic data do not reliably establish that an association process is occurring, although analogy with the kinetic data at low DMSO concentrations strongly suggests this is the case.

Independent proof of the occurrence of dimerization was obtained by measurement of the association constant using nuclear magnetic resonance spectroscopy. (The association constant is too small to be measured by use of ultraviolet spectroscopy as described above.) In CCl_4–DMSO solvent mixtures, the N_1 proton of 2-pyridone shows a concentration-dependent chemical

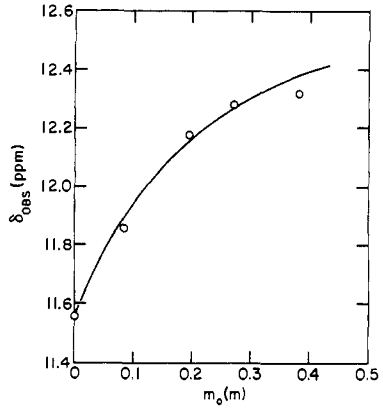


Figure 3. Observed chemical shift from tetramethylsilane (δ_{obsd}) *vs.* stoichiometric 2-pyridone molality (m_0) in carbon tetrachloride containing 1.1 *m* DMSO. The curve was drawn according to eq 10 with an association constant of 2 m^{-1}.

shift; increasing concentration causes a downfield shift, as expected for a hydrogen-bonded self-association. The observed resonance position for a given sample, δ_{obsd}, is the mean of the positions observed for monomer, δ_M, and dimer, δ_D, weighted with respect to the concentration of each species.[15]

$$\delta_{obsd} = \delta_D - [(m_M)/(m_0)](\delta_D - \delta_M) \qquad (10)$$

The standard shift for dimeric 2-pyridone was taken as that observed in a concentrated solution in carbon tetrachloride (δ 13.5), and the monomer peak was taken as that of a dilute solution of 2-pyridone in pure DMSO (δ 11.48). Since the equilibrium constant for the association of DMSO and 2-pyridone is large, the small concentration of monomeric 2-pyridone solvated by carbon tetrachloride can be assumed to make no appreciable contribution to the position of proton absorption.[15]

A typical plot of chemical shift *vs.* total 2-pyridone concentration is shown in Figure 3. Since m_M is a known function of the equilibrium constant and m_0 is known, a value of the equilibrium constant can be calculated for each measurement of the chemical shift. The curve in Figure 3 was drawn according to eq 10, using the average equilibrium constant determined from the individual points. The good fit of the calculated line to the data attests to the validity of the values used for δ_M and δ_D. The equilibrium constants obtained by this method are included in Table IV. They are in reasonable agreement with those determined from the kinetic data, and therefore support the postulate that the observed relaxation process is associated with dimerization.

The amplitude of the relaxation process in DMSO–CCl_4 mixtures can also be interpreted according to eq 8, and the values of $(\Delta V° - \beta\Delta H°/\rho c_p)$ averaged over the concentrations of 2-pyridone are included in Table IV. The kinetically determined association constants were used to evaluate Γ. Also included are the values of $\Delta H°$ calculated on the premise that $\Delta V°$ is negligible, although, as will be discussed later, this is probably not a valid procedure in this case. Again values of β and ρ were determined experimentally for each solvent and c_p was calculated as the weighted mean of that for carbon tetrachloride (0.203 cal/g deg) and DMSO (0.7 cal/g deg).

Specific solvation of monomeric 2-pyridone by DMSO in carbon tetrachloride was measured by infrared spectroscopy.[16] The sulfoxide group in carbon tetrachloride absorbs at 1070 cm^{-1} and a calibration curve of absorbancy *vs.* DMSO concentration was made from 1.9×10^{-2} to 1.9×10^{-1} *m* DMSO. Hydrogen-bonded sulfoxide groups do not absorb at this frequency, and on the addition of 4.86×10^{-2} *m* 2-pyridone to the above solutions, a decrease in absorbancy was observed. The molality of free and hydrogen-bonded DMSO could then be readily determined by use of the calibration curve described above. The hydrogen-bonded DMSO was assumed to be in the form of a 1:1 complex with 2-pyridone at the concentrations studied (the analysis of the kinetic data given later is also consistent with this assumption); the 2-pyridone not solvated by DMSO was assumed to be distributed as monomers and dimers (eq 1) with an association constant of 1650 m^{-1}, the measured value in pure carbon tetrachloride. Hence the concentrations of monomeric 2-pyridone, 1:1 complex with DMSO, and unbonded DMSO, could be calculated for each of the stoichiometric concentrations of DMSO used, and a value for the association constant could be calculated at each DMSO concentration. The average value of this constant is 65 ± 10 m^{-1}. The estimated error in this constant is probably somewhat greater than the experimental average deviation cited.

Discussion

A simple mechanism for dimer formation in weakly hydrogen bonding solvents is shown by eq 11,[4] where

$$\mathrm{A} + \mathrm{A} \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} \mathrm{A}\cdots\mathrm{A} \underset{k_{32}}{\overset{k_{23}}{\rightleftharpoons}} \overset{\frown}{\mathrm{AA}} \underset{k_{43}}{\overset{k_{34}}{\rightleftharpoons}} \overset{\frown}{\underset{\smile}{\mathrm{AA}}} \qquad (11)$$

$\mathrm{A}\cdots\mathrm{A}$ is the initial complex which forms and breaks down at diffusion-controlled rates, $\overset{\frown}{\mathrm{AA}}$ is the dimer having one hydrogen bond, and $\overset{\frown}{\underset{\smile}{\mathrm{AA}}}$ is the cyclic dimer. If the two intermediates are assumed to be in a steady state, then the measured association rate constant is

$$k_f = \frac{k_{12}}{1 + (k_{21}/k_{23})(1 + k_{32}/k_{34})} \qquad (12)$$

and the dissociation rate constant is

$$k_r = \frac{k_{43}}{1 + (k_{34}/k_{32})(1 + k_{23}/k_{21})} \qquad (13)$$

Previous work has suggested that the association rate is diffusion controlled,[5-9] *i.e.*, $k_f \approx k_{12}$. This implies that $k_{23} \gg k_{21}$ or $k_{23} \gg 10^{10}$ sec^{-1}. If this is the case

$$k_r = k_{21}k_{32}k_{43}/(k_{23}k_{34}) \qquad (14)$$

Since the diffusion-controlled dissociation rate, characterized by k_{21}, is roughly solvent independent, the effects of various solvents on the dissociation rate must be due to variations in the equilibrium constants of the second two steps.

This simple mechanism adequately accounts for the results obtained in $CHCl_3$–DMSO mixtures. Inspection of Table III indicates that k_f does not depend

---

(15) C. M. Huggins, G. C. Pimentel, and J. N. Shoolery, *J. Phys. Chem.*, 60, 1311 (1956).

(16) J. J. Lindberg and C. Majani, *Suom. Kemistilehti B*, 37 (2), 21 (1964).

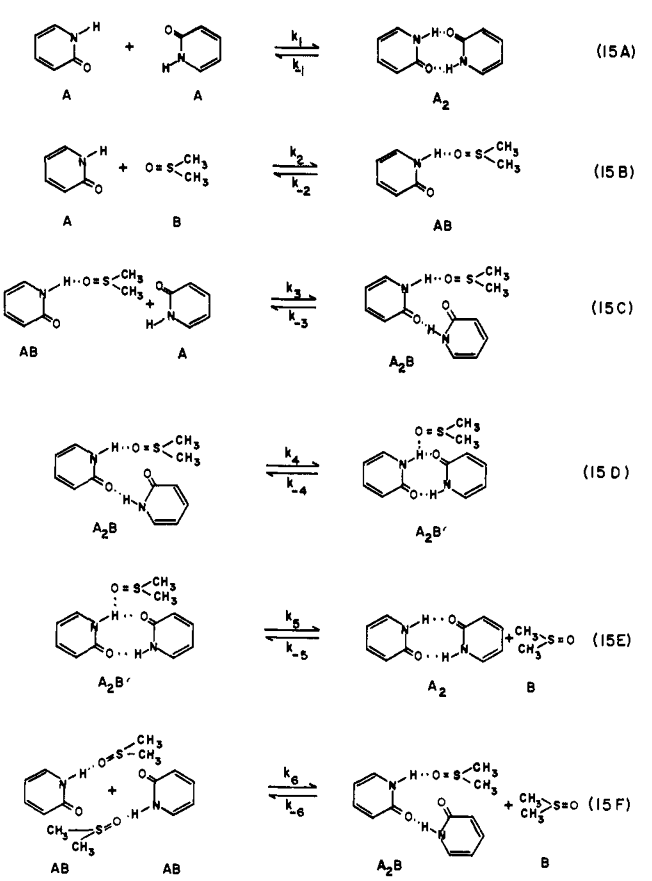


Figure 4. Mechanism for the dimerization of 2-pyridone in CCl_4–DMSO mixtures (eq 15).

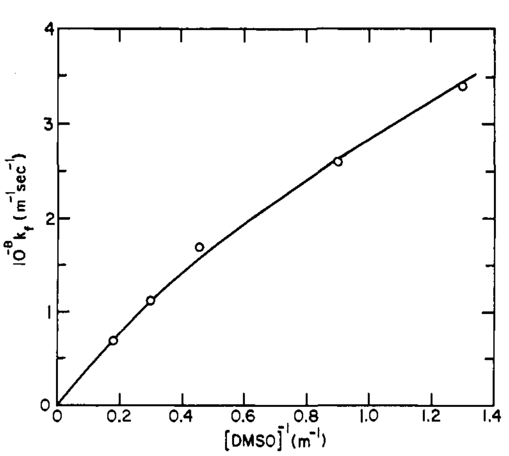


Figure 5. Rate constant for dimer formation (k_f) *vs.* reciprocal DMSO molality in carbon tetrachloride. The curve was drawn according to eq 17 with the parameters given in Table V.

significantly on solvent composition, and the rate constant is large enough to be considered characteristic of a diffusion-controlled process. On the other hand, the values of k_r show an increase as DMSO is added, suggesting that the hydrogen bonds between two 2-pyridone molecules in the dimeric species are destabilized by DMSO, which competes favorably for the hydrogen bonding sites. However, this competition is not simple since it is mediated by the fact that chloroform can hydrogen bond to both dimethyl sulfoxide and 2-pyridone.

This mechanism is also consistent with the calculated enthalpies of reaction which, as expected, become less negative as the dimethyl sulfoxide concentration increases.

The mechanism of eq 11 is not adequate to explain the results obtained in CCl_4–DMSO mixtures. In this solvent both rate constants are dependent on the DMSO concentration, and we have been unable to explain the observed concentration dependence with any simple modification of eq 6. A mechanism is needed which specifically includes the interactions of DMSO and 2-pyridone. The simplest mechanism we have found which is sufficient to account for the experimental results is shown in Figure 4. In Figure 4, A is 2-pyridone, B is DMSO, A_2B is a solvated single hydrogen-bonded dimer, and A_2B' is a solvated double (cyclic) hydrogen-bonded dimer. This mechanism includes reactions between all possible simple DMSO–2-pyridone species.

This mechanism is associated with four relaxation times.[12] The fact that within experimental error only one is observed can be explained if the three following conditions prevail. First, the association of pyridone with DMSO (15B) is rapid relative to the observed relaxation process, *i.e.*, $1/\tau > \sim 10^9$ sec^{-1}. If the forward rate is diffusion controlled, then this would be true at the DMSO concentrations used. This is a quite reasonable expectation. In a similar vein the second assumption needed is that the step associated with the solvation and desolvation of the cyclic dimer (15E) is relatively rapid. This can also be rationalized if the reverse rate is diffusion controlled and/or if $k_5 > 10^9$ sec^{-1}. Finally the intermediate A_2B is assumed to be present at sufficiently low concentrations so that the steady-state approximation can be applied. Previous equilibrium studies of similar systems have suggested this species should be present in very low concentrations.[16]

With the application of the above constraints, the observed rate constant for formation of dimers is given by eq 16, where the small letters designate rate constants

$$k_f = \frac{k_3k_4K_2(B) + k_4k_6K_2^2(B)^2}{[1 + K_2(B)]^2[k_{-3} + k_{-4} + k_{-6}(B)]} + \frac{k_1}{[1 + K_2(B)]^2} \qquad (16)$$

and the capital letters equilibrium constants. The last term can be neglected since even if k_1 has its maximum value, the infrared results indicate that $K_2 > 10\ m^{-1}$. Also since $K_2(B) \gg 1$, $[1 + K_2(B)]^2 \simeq K_2^2(B)^2$ and

$$k_f = \frac{k_3k_4/[K_2(k_{-3} + k_4)]}{(B)[1 + k_{-6}(B)/(k_{-3} + k_4)]} + \frac{k_4k_6/(k_{-3} + k_4)}{1 + k_{-6}(B)/(k_{-3} + k_4)} \qquad (17)$$

A plot of k_f *vs.* $1/(B)$ is shown in Figure 5. According to eq 17 three parameters are available to fit this data. At high concentrations of DMSO, the limiting slope of this plot is k_4k_6/k_{-6}. This establishes the value of one of the parameters, and the other two have been obtained by trial and error. The line in Figure 5 has been drawn according to eq 17 with the parameters given in Table V. The fit of the data is quite adequate.

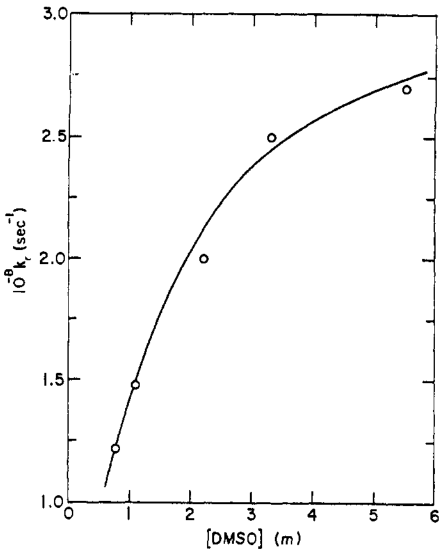


Figure 6. Rate constant for dimer dissociation (k_r) *vs.* DMSO molality in carbon tetrachloride. The curve was drawn according to eq 18 with the parameters given in Table V.

The dissociation rate constant for this mechanism is

$$k_r = \frac{(k_{-4}(\mathrm{B})/K_5)[k_{-3}/(k_{-3}+k_4)+k_{-6}(\mathrm{B})/(k_{-3}+k_4)]}{[1+(\mathrm{B})/K_5][1+k_{-6}(\mathrm{B})/(k_{-3}+k_4)]} + \frac{k_{-1}}{1+(\mathrm{B})/K_5} \quad (18)$$

The second term can again be shown to be negligible since K_1 ($=k_1/k_{-1}$) is known from equilibrium measurements (1650 m^{-1}) and the maximum value of k_1 is $\sim 3 \times 10^9$ m^{-1} sec^{-1} (diffusion-controlled limit). Therefore, the maximum value of k_{-1} is $\sim 2 \times 10^6$ sec^{-1}, which is small compared with the measured dissociation rate constants. The dependence of k_r on DMSO concentration (eq 18) is characterized by four parameters, but one of these has already been determined by the dependence of k_f on concentration. A plot of k_r *vs.* DMSO concentration is shown in Figure 6. The limiting value of k_r at high concentrations is k_{-4}, and this can be determined from the data quite well. The other two parameters were determined by a trial and error procedure to give a good fit of the data. The line in Figure 6 has been calculated according to eq 18 with the parameters given in Table V.

Table V. Rate and Equilibrium Constants for the Dimerization of 2-Pyridone in CCl_4–DMSO at 25° (eq 15)

Constant	Value	Source
$k_3k_4/K_2(k_{-3}+k_4)$	1.0×10^8 sec^{-1}	Fit of k_f
$k_{-6}/(k_{-3}+k_4)$	1.4 m^{-1}	Fit of k_f
$k_4k_6/(k_{-3}+k_4)$	5.9×10^9 m^{-1} sec^{-1}	Fit of k_f
$k_{-3}/(k_{-3}+k_4)$	0.1	Fit of k_r
k_{-4}	3.3×10^8 sec^{-1}	Fit of k_r
K_5	4.3×10^{-1} m	Fit of k_r
K_1	1650 m^{-1}	Uv measurements
K_2	52 m^{-1}	Calcd
	65 m^{-1}	Ir measurements
k_3	5.7×10^9 m^{-1} sec^{-1}	Calcd
k_{-3}	$k_4/9$	Calcd
k_6	6.4×10^8 m^{-1} sec^{-1}	Calcd
k_{-6}	$1.1k_4$	Calcd

A number of detailed balance relationships exist among the equilibria of eq 15. For example, $k_r/k_f = [1 + K_2(\mathrm{B})]^2/K_1[1 + (\mathrm{B})/K_5]$. Since K_1 has been determined independently and K_5 has been estimated from the kinetic data, K_2 can be calculated from the equilibrium data. The value obtained, 52 m^{-1}, is included in Table V and agrees quite well with the value estimated from the infrared data, 65 m^{-1}. A number of individual rate constants can also be calculated from the data and are included in Table V.

Throughout this analysis, the concentration of free DMSO has been assumed to be equal to the stoichiometric concentration. This approximation is quite adequate for high DMSO concentration; at the highest 2-pyridone and lowest DMSO concentrations, this approximation is in error by $\sim$20%. Since this is the region in which the measured relaxation times are least sensitive to solvent composition (Figure 2), a more exact treatment is not necessary.

The proposed mechanism provides a consistent fit of all of the equilibrium and kinetic data. The assumption made that A_2B (the singly hydrogen-bonded dimer) is in a steady state is consistent with the calculated constants since $k_4 = 9k_{-3}$, $k_4 \approx k_{-6}$, and the possibility exists that $k_5 \gg k_{-4}$, which implies the concentration of A_2B can be small. Although three paths exist for formation of the double hydrogen-bonded dimer, the path involving two unsolvated 2-pyridone molecules is not important at the concentrations of DMSO employed. As expected at a standard DMSO concentration such as 1 m the formation of the dimer from two AB molecules ($K_4K_6K_5 = (\mathrm{A_2})(\mathrm{B})^2/(\mathrm{AB})^2 = 1.2$ m) is thermodynamically less favorable than the formation from A and AB ($K_3K_4K_5 = (\mathrm{A_2})(\mathrm{B})/(\mathrm{AB})(\mathrm{A}) = 61$), which in turn is less favorable than formation from two unsolvated 2-pyridone molecules ($K_1 = (\mathrm{A_2})/(\mathrm{A})^2 = 1650$ m^{-1}).

The rate-limiting step for the dissociation process at high DMSO concentrations (k_{-4}) is the substitution of a DMSO–2-pyridone hydrogen bond for a 2-pyridone–2-pyridone hydrogen bond. The corresponding rate-determining step for the association process (k_4) is the reverse of this process, *i.e.*, desolvation. The apparent bimolecular rate constant at high DMSO concentrations is $k_4k_6/k_{-6}(\mathrm{B})$ $(=4.2 \times 10^8/(\mathrm{B})$ m^{-1} sec^{-1}). The actual second-order rate constants for the elementary steps of dimerization are k_1, k_3, and k_6. Although k_1 could not be determined, analogy with other results in "inert" solvents suggests this dimerization process is diffusion controlled;[5-9] similarly the value of k_3 suggests a diffusion-controlled process is involved in this step. The value of k_6 is slightly less than that usually expected for a diffusion-controlled process, but the experimental uncertainty is such that it cannot be reliably stated whether the reaction associated with this rate constant is or is not diffusion controlled.

The values of $\Delta H°$ for the dimerization process, calculated on the assumption of a negligible value for $\Delta V°$, become more negative as DMSO concentration is increased (Table IV). Clearly this is an unreasonable trend. In all probability, the addition of DMSO causes ΔV° to increase while ΔH° approaches zero, and $(\Delta V^\circ - \beta\Delta H^\circ/\rho c_p)$ remains roughly constant.

The question must now be answered as to why the observed kinetic behavior is markedly different in CCl_4–DMSO compared to $CHCl_3$–DMSO. Obviously the difference must be due to the relative hydrogen bonding capabilities of chloroform and carbon tetrachloride. Chloroform is known to form weak hydrogen bonds;[3] *e.g.*, the association constant between DMSO and chloroform in carbon tetrachloride has been estimated to be 31 M^{-1}.[17] This accounts for the lower stability of the dimer in chloroform relative to carbon tetrachloride. The differences in kinetic behavior in CCl_4–DMSO and $CHCl_3$–DMSO, imply that the breakdown and formation of a DMSO–2-pyridone hydrogen bond in the dimer is more rapid in chloroform than in carbon tetrachloride. This is probably due to the fact that this step is facilitated by simultaneous formation or breakdown of a hydrogen bond between DMSO and chloroform.

The pertinence of these models to biological processes is, of course, an open question. This work shows that solvation–desolvation processes can become rate limiting in hydrogen bond formation and breakdown. However, in this particular case a quite inert environment is required. Conceivably, hydrophobic pockets in proteins might provide such an environment. Rate constants for desolvation in water of molecules containing hydrophobic groups have been measured,[18] and are $\sim 10^8$ sec^{-1}, similar to the corresponding rate constants reported here. Thus this work may be of relevance in understanding biological processes. In any event, the mechanism of hydrogen-bonded dimerization has now been studied in a variety of solvent systems and can be understood in terms of the underlying elementary steps.

---

[17] P. Biscanni, L. Lunazzi, and F. Taddei, *Boll. Sci. Fac. Chim. Ind. Bologna*, 22 (3–4), 67 (1964).

[18] G. G. Hammes and W. Knoche, *J. Chem. Phys.*, **45**, 4041 (1966)

Communications to the Editor

Preparation of Lithium Nonahydrotetraborate

Sir:

Pentaborane(9),[1-3] hexaborane(10),[4,5] and decaborane(14)[6-8] have been shown to be Brønsted acids. The acid hydrogen atoms in these boranes occupy bridge positions. Shore, *et al.*,[4,5] have shown that the Brønsted acidity decreases in the order $B_{10}H_{14} > B_6H_{10} > B_5H_9$. The relative acidity of the hydrogen atoms in diborane(6)[9-14] is still in doubt. Kodama[15] found that ether solutions of tetraborane(10) absorbed ammonia reversibly at low temperature and suggested that addition was on bridge positions. In the present study we confirm this suggestion and show that tetraborane(10) is a Brønsted acid and that the acid hydrogen atom occupies a bridge position.

Ether solutions of methyllithium and tetraborane(10) were condensed together in a tube at −196°. The tube was sealed and warmed to −78°. A moderate amount of bubbling took place and the reaction was complete after 90 min. The tube was opened and the material volatile at −196° was shown to be pure methane by its infrared spectrum and its −196° vapor pressure (10.0 Torr). Reaction yields were calculated by taking the ratio (millimoles of methane produced)/(millimoles of tetraborane(10) used). The molar excess of methyllithium varied from 0 to 2 *M*. Fourteen reactions yielded amounts of methane corresponding to 78–98% of the theoretical. The average yield for the 14 reactions was 89.5%. Optimum yields were obtained when no less than a 20% excess of methyllithium was used and when the initial 2.3 *M* methyllithium solution in ethyl ether was diluted with no less than a 40% additional volume of ether. The equation for the reaction is $B_4H_{10} + LiCH_3 \rightarrow LiB_4H_9 + CH_4$. While LiB_4H_9 is stable at −78°, it slowly decomposes at temperatures as low as −63°.

Lithium nonahydrotetraborate reacts with gaseous HCl and DCl at −78° to produce B_4H_{10} and B_4H_9D, respectively. The presence of a single deuterium atom in the latter substance was confirmed by mass spectral analysis. Four infrared spectra of B_4H_9D taken over a period of 40 min after its initial generation indicated that deuterium was originally present in a bridge position, but that ultimately intramolecular exchange takes place. This was previously observed by Norman and Schaeffer.[16]

Neither B_2H_6 nor B_5H_9 reacts with LiB_4H_9 in ether at −78°. Decaborane(14) reacts under these conditions to produce B_4H_{10}. The solution at the end of this reaction was an intense lemon-yellow color, characteristic of the $B_{10}H_{13}^-$ anion. Pentaborane(9) was obtained when ether solutions of LiB_5H_8 and B_4H_{10} were brought together. Thus it appears that B_4H_{10} is a

---

[1] D. F. Gaines and T. V. Iorns, *J. Amer. Chem. Soc.*, **89**, 3375 (1967).

[2] R. A. Gaenangel and S. G. Shore, *ibid.*, **89**, 6771 (1967).

[3] T. Onak, G. B. Dunks, I. W. Searcy, and J. Spielman, *Inorg. Chem.*, **6**, 1465 (1967).

[4] H. D. Johnson, II, S. G. Shore, N. L. Mack, and J. C. Carter, *J. Amer. Chem. Soc.*, **91**, 2131 (1969).

[5] H. D. Johnson, II, R. A. Gaenangel, and S. G. Shore, *Inorg. Chem.*, **9**, 908 (1970).

[6] R. W. Parry and L. J. Edwards, *J. Amer. Chem. Soc.*, **81**, 3554 (1959).

[7] M. F. Hawthorne and J. J. Miller, *ibid.*, **80**, 754 (1958).

[8] J. J. Miller and M. F. Hawthorne, *ibid.*, **81**, 4501 (1959).

[9] R. A. Ogg, *J. Chem. Phys.*, **22**, 1933 (1954).

[10] C. W. Kearn and W. N. Lipscomb, *ibid.*, **37**, 275 (1962).

[11] W. E. Palke and W. N. Lipscomb, *ibid.*, **45**, 3948 (1966).

[12] E. Switkes, R. M. Stevens, and W. N. Lipscomb, *ibid.*, **51**, 2085 (1969).

[13] F. P. Boer, M. D. Newton, and W. N. Lipscomb, *J. Amer. Chem. Soc.*, **88**, 2361 (1966).

[14] L. C. Cusachs and P. Politzer, *Chem. Phys. Lett.*, **1**, 529 (1968).

[15] G. Kodama, Ph.D. Dissertation, University of Michigan, 1957.

[16] A. D. Norman and R. Schaeffer, *Inorg. Chem.*, **4**, 1225 (1965).